Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-15. (cancelled)

16. (currently amended) A recombinant nucleic acid molecule encoding a modified type 14 pneumolysin polypeptide comprising one or more amino acid substitutions in a wild-type pneumolysin polypeptide having the amino acid sequence of SEQ ID NO:3, wherein said one amino acid substitution occurs at a position selected from the group consisting of position 61, 148, and 195, or wherein said more than one amino acid substitution occurs at positions selected from the group consisting of 17, 18, 33, 41, 45, 46, 61, 63, 66, 83, 101, 102, 128, 148, 189, 195, 239, 243, 255, and 257, and wherein said modified pneumolysin polypeptide is soluble, elicits antibodies which are cross-reactive with wild-type pneumolysin, and has attenuated hemolytic activity~~wherein at least one amino acid in the region comprising amino acid residues 1 to 257 is substituted and wherein at least one of said amino acid substitutions results in attenuation of the hemolytic activity of the modified pneumolysin polypeptide~~.

17. (currently amended) The recombinant nucleic acid molecule according to claim 16 comprising the ~~following~~ pneumolysin nucleic acid sequence of SEQ ID NO: 1, [[:]]

~~ATGGCAAATA AAGCAGTAAA TGACTTTATA CTAGCTATGA 40~~
~~ATTACGATAA AAAGAAACTC TTGACCCATC AGGGAGAAAG 80~~
~~TATTGAAAAT CGTTTCATCA AACAGCGTAA TCAGCTACCC 120~~
~~GATGAGTTTG TTGTTATCGA AACAAAGAAG CGGAGCTTGT 160~~
~~CGACAAATAC AAGTGATATT TCTGTAACAG CTACCAACGA 200~~
~~CAGTCGCCTC TATCCTGGAG CACTTCTCGT AGTGGATGAG 240~~
~~ACCTTGTTAC AGAATAATCC CACTCTTCTT GCGGTCGATC 280~~
~~GTGCTCCGAT GACTTATAGT ATTGATTTGC CTGGTTTGGC 320~~
~~AAGTAGCGAT AGCTTTCTCC AAGTGGAAGA TCCCAGCAAT 360~~
~~TCAAGTGTTC GCGGAGCGGT AAACGATTTG TTGGCTAAGT 400~~
~~GGCATCAAGA TTATGGTCAG GTCAATAATG TCCCAGCTAG 440~~
~~AATGCAGTAT CAAAAAATCA CGGCTCACAG CATGGAACAA 480~~
~~CTCAAGGTCA AGTTTCGTTC TGACTTTGAA AAGACAGGGA 520~~
~~ATTCTCTTGA TATTGATTTT AACTCTGTCC ATTCAGGCGA 560~~
~~AAAGCAGATT CAGATTGTTA ATTTTAAGCA GATTTATTAT 600~~
~~ACAGTCAGCG TAGACGCTGT TAAAAATCCA GGAGATGTGT 640~~
~~TTCAAGATAC TGTAACGGTA GAGGATTTAA AACAGAGAGG 680~~
~~AATTTCTGCA GAGCGTCCTT TGGTCTATAT TTCGAGTGTT 720~~
~~GCTTATGGGC GCCAAGTCTA TCTCAAGTTG GAAACCACGA 760~~
~~GTAAGAGTGA TGAAGTAGAC GCTGCTTTTG AAGCTTTGAT 800~~
~~AAAAGGAGTC AAGGTAGCTC CTCAGACAGA GTGGAAGCAG 840~~
~~ATTTTGGACA ATACAGAAGT GAAGCCGGTT ATTTTAGGGG 880~~
~~GCGACCCAAG TTCGGGTGCC CGAGTTGTAA CAGGCAAGGT 920~~

~~GCATATGGTA GAGGACTTGA TTCAAGAAGG CAGTCGCTTT 960~~
~~ACAGCAGATC ATCCAGGCTT GCCGATTTCC TATACAACTT 1000~~
~~CTTTTTTACG TGACAATGTA GTTGCGACCT TTCAAAATAG 1040~~
~~TACAGACTAT GTTGAGACTA AGGTTACAGC TTACAGAAAC 1080~~
~~GCAGATTTAC TGCTGGATCA TACTGGTGCC TATGTTGCCC 1120~~
~~AATATTATAT TACTTGGAAT GAATTATCCT ATGATCATCA 1160~~
~~AGGTAAGGAA GTCTTGACTC CTAAGGCTTG CGACAGAAAT 1200~~
~~GGGCAGGATT TAACGGCTCA CTTTACCACT AGTATTCCTT 1240~~
~~TAAAAGGGAA TGTTCGTAAT CTCTCTGTCA AAATTAGAGA 1280~~
~~GTGTACCGGG CTTGCTTGGC AATGGTGGCG TACGGTTTAT 1320~~
~~GAAAAAACCG ATTTGCCACT AGTGCGTAAG CGGACGATTT 1360~~
~~CTATTTGGGG AACAACTCTC TATCCGCAGG TAGAAGATAA 1400~~
~~GGTAGAAAAT GAC (SEQ ID NO:1) 1413~~

and wherein said nucleic acid sequence comprises one or more of the nucleotide substitutions selected from the group consisting of:

A-50→G, G-54→T, T-181→C, A-196→T and T-302→C;

A-122→G, A-514→G, T-583→A and A-764→G;

A-187→T, T-380→A, A-382→C and T-443→A;

T-98→C, T-137→C, T-248→C, T-717→A and A-770→G;

T-134→C, A-305→G, A-566→G and T-583→G;

T-583→G;

T-583→A;

T-443→A;
and
T-181→C.

18. (currently amended) The recombinant nucleic acid molecule of claim 16 as contained in a vector ~~such a plasmid, cosmid, bacteriophage or yeast artificial chromosome~~.

19. (original) A microorganism comprising the nucleic acid molecule of claim 16.

20. (currently amended) The microorganism according to claim 19, wherein the microorganism is selected from the group consisting of: bacteria, yeast, mammalian [[or]]and insect cells.

21. (currently amended) The microorganism according to claim 20, wherein the microorganism is *E. coli* ~~E. coli~~.

22-26. (cancelled)

27. (currently amended) A method for killing bacteria comprising contacting said bacteria with antibodies to an immunogenic molecule comprising [[the]]a modified pneumolysin comprising one or more amino acid substitutions in a wild-type pneumolysin polypeptide having the amino acid sequence of SEQ ID NO:3, wherein said one amino acid substitution occurs at a position selected from the group consisting of position 61, 148, and 195, or wherein said more than one amino acid substitution occurs at positions selected from the group consisting of 17, 18, 33, 41, 45, 46, 61, 63, 66, 83, 101, 102, 128, 148, 189, 195, 239, 243, 255, and 257, and wherein said modified pneumolysin polypeptide is soluble, elicits antibodies which are cross-reactive with wild-type pneumolysin, and has attenuated hemolytic activity~~according to claim 1~~ in the presence of complement.

28. (original) The method according to claim 27, wherein the immunogenic molecule is a polysaccharide-polypeptide conjugate wherein the polysaccharide is a bacterial capsular polysaccharide.

29. (currently amended) A method for immunization of mammals comprising administering [[the]]a vaccine ~~of~~ comprising the modified pneumolysin polypeptide comprising one or more amino acid substitutions in a wild-type pneumolysin polypeptide having the amino acid sequence of SEQ ID NO:3, wherein said one amino acid substitution occurs at a position selected from the group consisting of position 61, 148, and 195, or wherein said more than one amino acid substitution occurs at positions selected from the group consisting of 17, 18, 33, 41, 45, 46, 61, 63, 66, 83, 101, 102, 128, 148, 189, 195, 239, 243, 255, and 257, and wherein said modified pneumolysin polypeptide is soluble, elicits antibodies which are cross-reactive with wild-type pneumolysin, and has attenuated hemolytic activity ~~of claim 24~~ and a pharmaceutically acceptable carrier to said mammals.

30. (currently amended) A method for obtaining modified pneumolysin polypeptides, wherein said modified pneumolysin polypeptides have ~~having~~ reduced hemolytic activity and [[being]]are suitable for eliciting an immunogenetic response which is cross-reactive with wild-type pneumolysin comprising the steps of:

(a) ~~randomly~~ mutating a nucleic acid molecule encoding [[for]] wild-type pneumolysin to produce mutated nucleic acid molecules encoding modified pneumolysin polypeptides, wherein the modified pneumolysin polypeptides comprise one or more amino acid substitutions in a wild-type pneumolysin polypeptide having the amino acid sequence of SEQ ID NO:3, wherein said one amino acid substitution occurs at a position selected from the group consisting of position 61, 148, and 195, or wherein said more than one amino acid substitution occurs at positions selected from the group consisting of 17, 18, 33, 41, 45, 46, 61, 63, 66, 83, 101, 102, 128, 148, 189, 195, 239, 243, 255, and 257 and expressing the mutated nucleic acid molecules in host cells;

(b) assaying the modified polypeptide expressed by the host cells for hemolytic activity; and

(c) identifying the modified pneumolysin polypeptides having substantially similar molecular weight as native wild-type pneumolysin and which are refoldable.

31. (new) The recombinant nucleic acid molecule of claim 16, wherein the vector ~~is~~ selected from the group consisting of: a plasmid, cosmid, bacteriophage and yeast artificial chromosome.